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Enhanced ectodysplasin-A receptor (EDAR) signaling alters multiple fiber characteristics to produce the East Asian hair form

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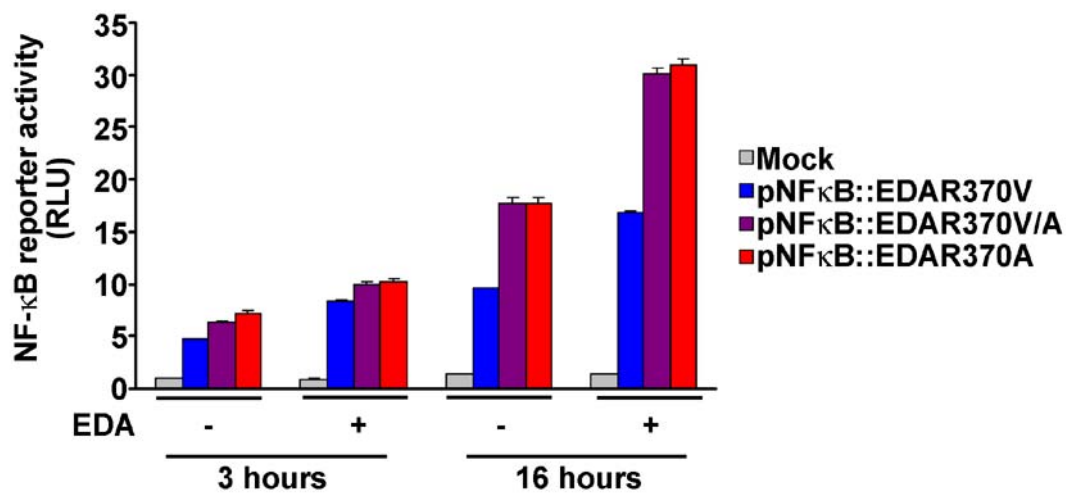
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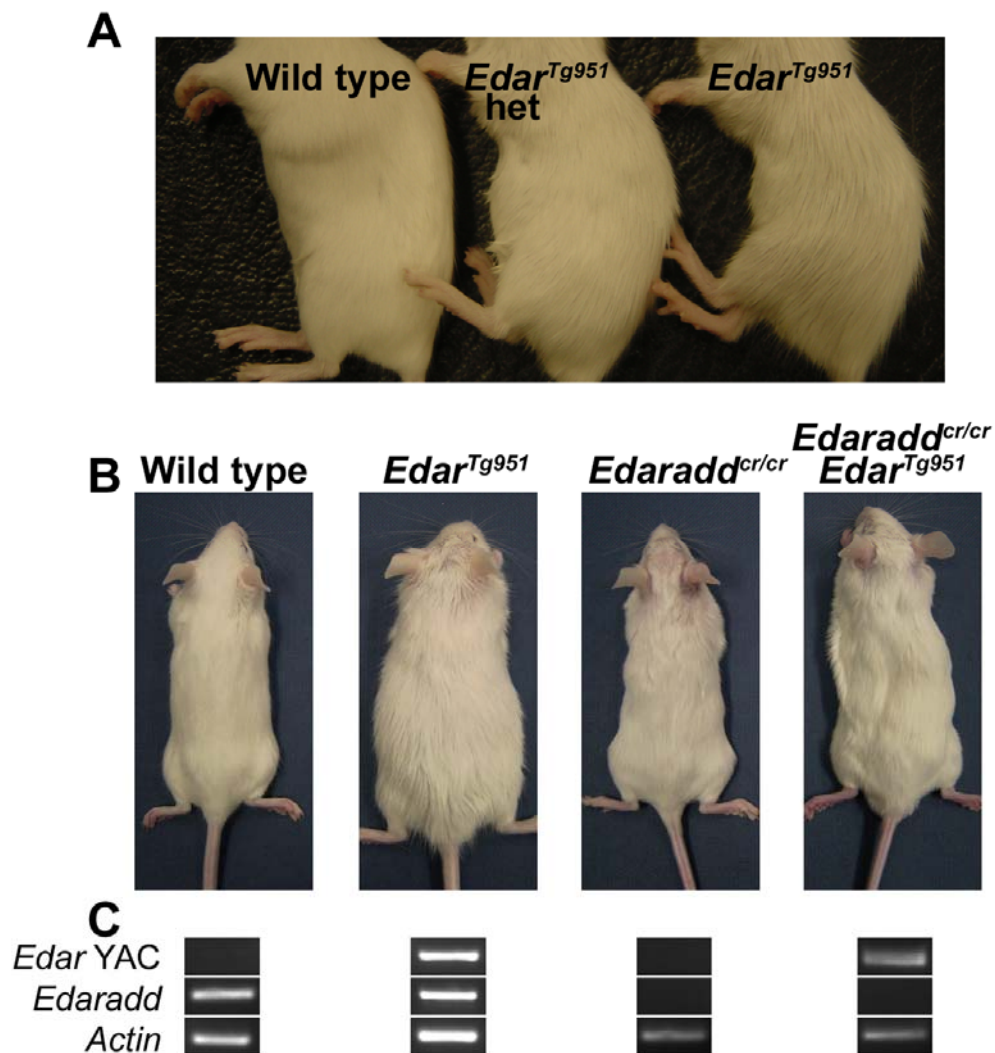
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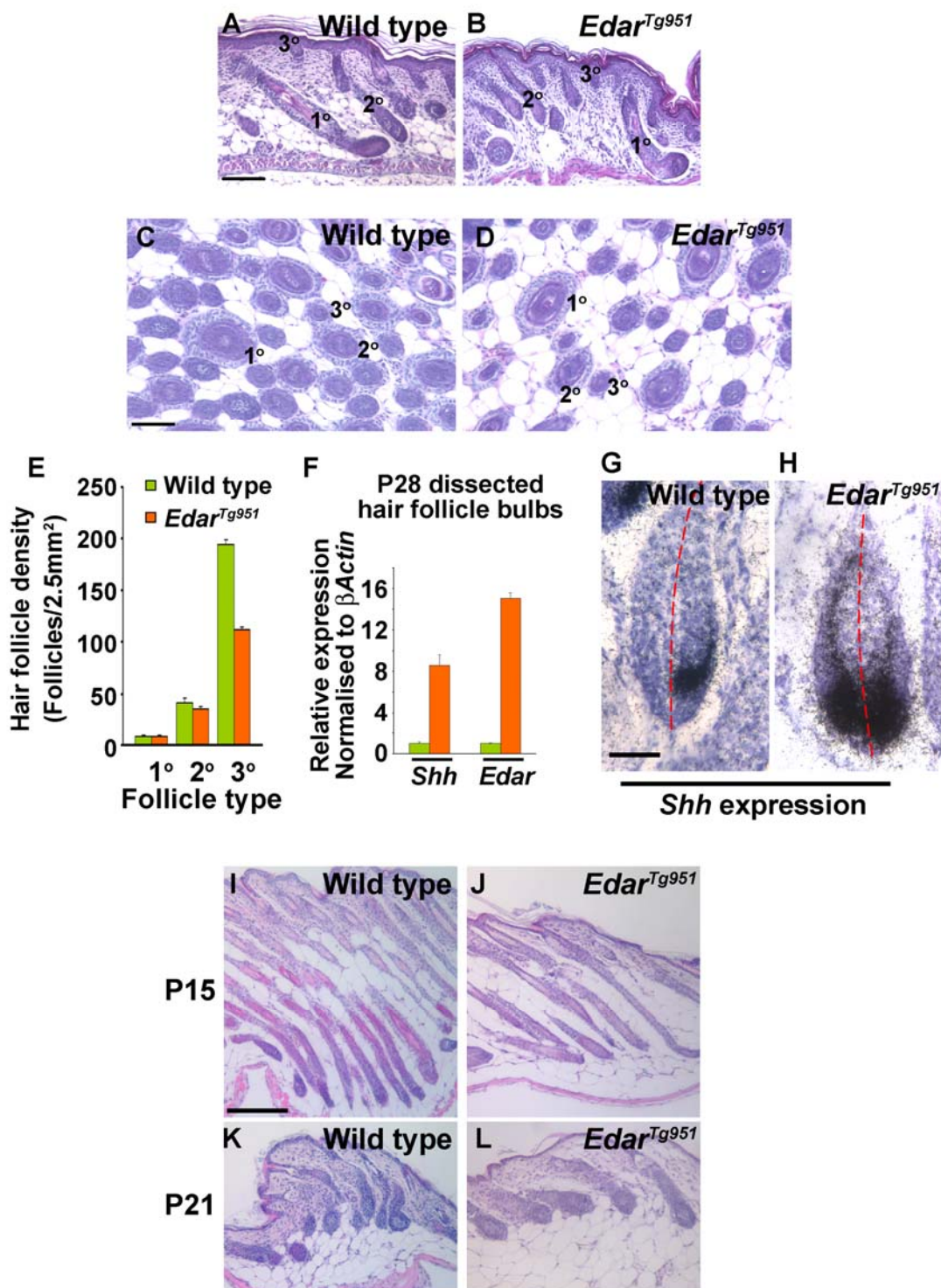
Supplementary Figure S1. EDAR370A displays more potent signaling than EDAR370V under autoregulatory conditions. EDAR370V and EDAR370A were expressed from an NF- κ B responsive promoter. 100 ng/ml EDA was added to medium 12 hours post-transfection and NF- κ B responsive luciferase reporter activity was measured 3 or 16 hours after EDA administration. Error bars indicate s.e.m.



Supplementary Figure S2. Dose effect of the *Edar*^{Tg951} phenotype and its suppression by mutation of *Edaradd*. **A:** Gross appearance of wild type; *Edar*^{Tg951} heterozygous (labelled *Edar*^{Tg951} het) and *Edar*^{Tg951} homozygous (labelled *Edar*^{Tg951}) mice. Elevated expression of *Edar* in the heterozygous transgenic produces a coarse hair coat, though not to the extent seen in the homozygote. **B:** Gross appearance of: wild type; *Edar*^{Tg951}; *Edaradd*^{cr/cr} and *Edar*^{Tg951},*Edaradd*^{cr/cr} animals. The *Edaradd*^{cr/cr} and *Edar*^{Tg951},*Edaradd*^{cr/cr} mice have the same gross phenotype. **C:** PCR genotyping of the mice in **B**, detecting the *Edar* YAC transgene, *Edaradd* and *Actin* positive control.



Supplementary Figure S3. All hair follicle types are present in *Edar*^{Tg951} skin and cycle normally, though hair follicle density is reduced. A and B: Longitudinal sections of newborn mouse dorsal skin showing the presence of primary (1°), secondary (2°) and tertiary (3°) follicle primordia, formed in three distinct waves during development. Scale bar, 100 µm. **C and D:** Transverse sections of P28 dorsal skin. Three follicle sizes are indicated. Scale bar 100 µm. **E:** Quantification of the density of each hair follicle type in P28 wild type and *Edar*^{Tg951} skin. The density of tertiary follicles, which produce zigzag hairs, is reduced. In wild type skin tertiary follicles comprise 80% of the total, while this follicle type constitutes 72% of all follicles in transgenic skin. In humans, scalp hair density in Chinese and Korean subjects has been reported to be significantly lower than that of Europeans, but reports disagree regarding the relative hair density of African subjects (Lee, et al., 2002; Loussouarn, et al., 2005; Tsai, et al., 2002). The formation of follicles in distinct waves in mouse, in addition to the effect of postnatal skin growth on hair density, make it difficult to compare mechanisms of reduced hair density in mouse to human skin. **F:** Quantitative RT-PCR determination of *Shh* and *Edar* expression in dissected hair follicle bulbs at P28, normalized to *βActin* levels. Error bars show s.e.m. **G and H:** *Shh* expression in P28 anagen hair bulbs detected by in situ hybridisation. The dashed red line denotes the central axis of the follicle. **G:** Most wild type follicles have asymmetric *Shh* expression that is restricted to the matrix on one side of the dermal papilla. **H:** Hair bulbs of *Edar*^{Tg951} mice display a broader, symmetric *Shh* expression domain. Scale bar, 50 µm. **I-L:** Hair cycling characteristics of wild type and transgenic animals. **I and J:** Hair follicles enter catagen appropriately at P15 and **K and L:** are initiating the first anagen at P21. Scale bar, 200 µm.



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